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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,655	01/05/2006	J. Christopher Anderson	54A-000410US	3991

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EXAMINER	
GEBREYESUS, KAGNEW H	

ART UNIT	PAPER NUMBER
1656	

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12/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,655	ANDERSON ET AL.	
	Examiner	Art Unit	
	KAGNEW H. GEBREYESUS	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 29, 2009 to the Advisory Action dated August 13, 2009 has been entered. Applicants have amended claim 17 and 19 and 26. Claims 17-26 comprising the ORS of SEQ ID NO: 15 and the O-tRNA species of SEQ ID NO: 1, 2, 6, 7 or 12 are present for examination.

All objections and rejections not reiterated from the previous Office Action are hereby withdrawn.

Objection -Specification

The objection is necessitated by amendment to the claims.

This application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below. In particular, 37 CFR 1.821 (d) states: "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application".

In the instant case, the requirements are not met because in claims 17 (b and C) and

dependent claims thereof, the variants of leucyl O-tRNA further having at least two or more variations at positions 28 and 49 relative to the any leucyl tRNA are not assigned sequence identifiers in the text of the description or in the claims.

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately using SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO. Appropriate correction/clarification is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 and dependent claims 18, 26 are rejected for the recitation: "…at least 25% suppression activity in the presence of "a cognate synthetase" in response to a selector codon as compared to a control lacking the selector codon, and where the selector codon is a four base codon,…" stated in part (iv) of claim 17(b), (c).

Given that suppressor activity is evaluated based on the expression of a beta-lactamase gene comprising a suppressor codon, it is unclear how a suppression activity of 25% can be evaluated without a disclosure of the structure of the "cognate synthetase" to be used. Clarification is required. Is the cognate synthase a wild type leucyl tRNA synthetase? Is it SEQ ID NO: 15 or 16? Clarification is required.

Maintained - Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-26 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue:

"…claim 17 requires that the O-RS preferentially aminoacylates the O-tRNA with the selected amino acid. This functional limitation is read in view of the content of the specification that teaches how to construct, identify and produce suitable O-RS molecules with a suitable structures that have this functional limitation... The amended form of claim 17 requires that the leucyl-O-RS comprises at least 90% amino acid identity with a leucyl-O-RS of SEQ ID NO: 15 or 16. This high degree of amino acid sequence conservation, in combination with knowledge of O-RS secondary structure and active site conformation as known in the art (for example, as described in paragraphs 0191, 0192 and 0201-0206) clearly defines what can be included in a genus of suitable O-RS molecules. Similarly, the amended form of claim 26 is now limited to leucyl-O-RS species comprising at least 90% amino acid identity with a leucyl O-RS derived from *Methanobacterium thermoautotrophicum* in addition to preferentially aminoacylating the leucyl-O-tRNA. This high degree of sequence identity, in combination with the functional limitation and knowledge of O-tRS secondary structure clearly defines what can be included in a genus of suitable O-RS molecules. The amendments to claims 17 and 26 result in the O-RS

species being defined in both functional and structural terms. Applicants assert that this amendment removes any perceived …"

Applicant's argument has been carefully considered but not persuasive because the amendments to the claims are insufficient to overcome the lack of description for the following reasons:

The specification teaches the E. coli cells comprising the O-tRNA of SEQ ID NO: 1, 2, 6, 7 and 12 that comprise a consensus sequence and can preferentially be aminoacylated by the O-RS of SEQ ID NO: 15 or 16 with at least 25% suppressor activity in response to a selector codon.

However claims 17-26 encompass any cell comprising a translation system that comprises a genus of orthogonal leucyl-tRNAs (O-tRNAs) and a genus of leucyl-orthogonal tRNA synthetase (Leu-O-RS) comprising up to 10% sequence variation compared to the ORS of SEQ ID NO: 15 or 16 (claim 17) and conservative variants (claim 18) functionally defined as ORSs that preferentially aminoacylate said O-tRNAs with any selected amino acid.

Claim 19 is functionally described as any cell comprising an O-tRNA and O-RS that display at least 50% suppressor activity compared to the suppressor activity of the O-RS of SEQ ID NO: 15 or 16 when used with the O-tRNA of SEQ ID NO: 1, 2, 6, 7 or 12.

However the specification does not teach any identifying common structure for the genus of O-RSs with 90% identity to SEQ ID NO: 15 or 16 that guarantee at least 25% or 50% suppressor activity when used with the genus of claimed orthogonal tRNAs.

The structure of each orthogonal tRNA synthetase and O-tRNA wherein the O-RS preferentially aminoacylates a corresponding O-tRNA must be determined empirically using the

screening procedure disclosed in [0022]-[0027] of the specification (see also for example page 7).

Although the specification teaches using a consensus tRNA sequence derived from halobactirium species NRC-1, that is designed to render the tRNA 'orthogonal' to *E. coli* or an *E. coli* translation system, these tRNAs must be screened for, with ORS molecules to decipher suppressor activity and then compared to any of the O-tRNA comprising SEQ ID NO: 1, 2, 6, 7 or 12 and any of the ORS of SEQ ID NO: 15 and 16.

The skilled artisan cannot predict the structure of these O-tRNA and ORS because each O-tRNA/ORS pair with at least 25%-50% efficiency compared to the O-tRNA of SEQ ID NO: 1, 2, 6, 7 or 12 and the ORS of SEQ ID NO: 15 or 16 requires an empirical determination using the screening procedure stated above. Thus one of skill cannot predict the structure of the genus of O-tRNA/ORS encompassed in the claims based on a screening procedure.

Furthermore, claim 18 encompasses conservative variant of SEQ ID NO: 15. However according to the definition provided in the specification, the term 'conservative variant' encompasses sequences with 50% identity to SEQ ID NO: 15. The specification does not teach any structure/function correlation for any **Leu-O-tRS** sequence with such structural divergence while retaining the required degree of suppressor efficiency even when used with the O-tRNA of SEQ ID NO: 1, 2, 6, 7 or 12.

"Written Description" Requirement, M.P.E.P § 2163 with regard to biomolecules states that a biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by

a method of obtaining the claimed sequence. For example, even though a genetic code table would correlate a known amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of a naturally occurring mRNA or its corresponding cDNA. Cf. In re Bell, 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993), and In re Deuel, 51 F.3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995) (holding that a process could not render the product of that process obvious under 35 U.S.C. 103). The Federal Circuit has pointed out that under United States law, a description that does not render a claimed invention obvious cannot sufficiently describe the invention for the purposes of the written description requirement of 35 U.S.C. 112. Eli Lilly, 119 F.3d at 1567, 43 USPQ2d at 1405. Compare Fonar Corp. v. General Electric Co., 107 F.3d

Thus with the exception of the tRNAs of SEQ ID NO: 1, 2, 6, 7 and 12 that can be used with the ORS of SEQ ID NO: 15 or SEQ ID NO: 16 to incorporate a tritiated leucine in a suppressor codon placed in the beta lactamase gene with variable suppressor efficiencies, the specification does not convey to the skilled artisan that Applicants were in possession of cells comprising the broad genus of claimed O-tRNAs that can be aminoacylated with any amino acid (including any natural or unnatural amino acid) by a genus of ORSs comprising at least 90% sequence identity to SEQ ID NO: 15 or SEQ ID NO: 16 as broadly encompassed in the claims. Given this lack of description of representative species for the genus of ORS and O-tRNA to be aminoacylated in the claims, the specification does not sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Conclusion:

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656
11/29/2009

/Manjunath N. Rao /
Supervisory Patent Examiner, Art Unit 1657